REMARKS

The Office Action of September 10, 2002 presents the examination of claims 52-73 and 76-92. These claims are canceled herein, being replaced by new claims 83-120.

An interview with the Examiner was held on February 11, 2003. The cooperation of the Examiner in expediting prosecution of the present application is greatly appreciated.

Enablement

Claims 52-73 and 76-82 stand rejected under 35 U.S.C. § 112, first paragraph, for alleged lack of enablement. This rejection is respectfully traversed. Reconsideration and withdrawal thereof are requested.

The Examiner takes a position that claims limited to the specific Ad-rsvLuc compositions presented as working examples in the specification are enabled, but that the broad scope of viral vector and any route of administration were not.

During the interview, Applicants explained that, as to lentivirus, adenovirus and similarly structured viruses, the viral elements important for the gene delivery function of the vector resided in the terminal repeat portions of the viral vector.

As discussed in the interview, the present claims recite that the vector is one derived from a lentivirus, adenovirus, adeno-associated virus or replication defective adenovirus. Such viral vectors have a general structure similar to that of the Ad-rsvLuc vector exemplified in the specification, at least as to the terminal repeat elements of the vector. Applicants submit that the present application fully enables claims of such scope.

The present method claims recite delivery by administration to the heart tissue or heart cavity, as expressly exemplified in the specification (see, Example 8). The claims also recite injection directly into the heart tissue. This is described incidentally by the procedure of Example 8. The Examiner will note the description at page 22, in which the injection needle is inserted into the heart tissue, then withdrawn until the location of the needle tip in the heart cavity is confirmed by the observation of blood in the syringe. The Examiner should further note expression of gene product (β-galactosidase) in cells along the needle track was observed (page 22, last paragraph).

The pending method of delivery claims further recite administration via injection into a blood vessel of the heart. Applicants submit that this route of administration is enabled in that the state of the art at the time the invention was made

recognized this as a way to deliver genes to heart tissue. The specification describes administration to the coronary artery, providing a reference for details, at the last paragraph of page 11. Also, during the interview, Applicants provided a copy of a paper (Tang et al. "Vigilant vectors: adeno-associated virus with a biosensor to seitch on amplified therapeutic genes in specific tissues in life-threatening diseases", *Methods* Vol. 28 (2002) pp. 259-266) that described administration of a recombinant vector via injection into either the jugular vein or the tongue vein with the result of cardiac-specific expression via the mlc-2 promoter. Applicants submit that, on the basis of the evidence of the specification and the Tang paper, enablement of delivery claims reciting administration via heart blood vessels is enabled.

The present claims also recite that the promoter is one that is the myosin light chain - 2 (mlc-2) promoter, or one comprising the elements of that promoter that confer cardiac-specific expression, such elements being operatively linked in the order in which they are found in a mammalian mlc-2 promoter.

The Examiner has also argued that, Applicants' evidence of unexpected results previously submitted to overcome rejections based on prior art illustrates the unpredictability in the art and, given such unpredictability, the claims must be limited in their scope. Applicants submit that the present claims recite

elements of vector structure that confer sufficient predictability to the use of the invention and that such elements furthermore are commensurate with the showing of unexpected results of record. Applicants submit that the presently pending claims are fully enabled by the disclosure of the specification, taken with what was known at the time the present invention was made. Accordingly, the instant rejection of claims 52-73 and 76-82 under 35 U.S.C. § 112, first paragraph, should be withdrawn.

Comments on the Interview Summary

For purposes of the interview of February 11, 2003, Applicants provided proposed claims to the Examiner. In the Interview Summary the Examiner comments that possible prior art issues are raised by the breadth of the term, "mlc promoter" in a "viral vector" in the proposed claims.

As to "mlc promoter", the present claims clarify that the promoter is an mlc-2 promoter, or the elements thereof that confer cardiac-specific expression. As to "viral vector, the Examiner will recall that Applicants' arguments of unexpected results were essentially that, at the time the invention was made, the skilled artisan had learned that some element present in the terminal repeats of adenoviruses abolished tissue specificity of expression from a promoter that was thought to be

tissue specific in its expression in some other context. The present invention overcomes that lack of tissue-specific expression that occurs when adenovirus or similar vectors are used for *in vivo* expression of a gene. Applicants submit that the currently presented claims recite structural elements of the vector that are commensurate with Applicants' explanation of the unexpected results achieved by the invention and the evidence of record supporting such explanation.

Applicants submit that the present application well describes and claims patentable subject matter. The favorable action of withdrawal of the standing rejections and allowance of the application is respectfully requested.

Pursuant to the provisions of 37 C.F.R. §§ 1.17 and 1.136(a), Applicants respectfully petitions for a four (4) month extension of time for filing a response from the due date of an Appeal Brief in connection with the present application. The required fee of $725.00 is attached hereto.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37 C.F.R. §§1.16 or 1.17; particularly, extension of time fees.

Respectfully submitted,

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Attachment: Tang et al., Methods Vol. 28 (2002) pp. 259-266.